**REMARKS**

In the Office Action mailed April 13, 2007, Claims 1-20, 25-27, 30-31, 36-38 were withdrawn as a result of a restriction requirement. Additionally, Claim(s) 21 (in part), 22-24, 28-29, 32 (in part), 33-35, and 39-40 were rejected under 35 U.S.C. 103(a). This rejection will be discussed below. Claims 21 and 32 have been amended to reflect the cancellation, respectively, of Claims 27 and 38. Claim 21 has also been amended to reflect the fact that the hyperlipidemia addressed by the method is fasting hyperlipidemia. Support for this amendment can be found in ¶0029 where the lower bounds of the elevated serum lipids are values obtained from populations following an overnight fast. Claims 21-24, 28, 29, 32-35, 39 and 40 remain pending in the present application, and Applicants respectfully submit that these claims are in condition for allowance.

35 U.S.C. § 103(a) Rejection:

While the Applicant is confident that the Examiner is well acquainted with the requirements necessary to establish a *prima facie* case of obviousness, it is thought prudent to briefly review the required elements. Specifically, in order to meet the burden of establishing a *prima facie* case of obvious, the Patent Office must show that:

1) Each and every element of the invention as set forth in the claims is taught or suggested by the reference as modified;

2) that there is sufficient motivation contained in the reference itself or the knowledge of one of ordinary skill in the reference to modify or combine the reference; and

3) that one of ordinary skill in the art would find a sufficient likelihood of successfully making the modification or combination asserted.

Applicants respectfully submit that the Examiner has failed to satisfy these requirements with the asserted rejection. With this background in mind, the obviousness rejections provided by the Examiner will be reviewed.

*The McCleary Application (US Patent Application 2002/0132219A1)*

The instant clams are directed to a method for treating, preventing, or normalizing fat maldistribution or hyperlipidemia resulting from anti-retroviral treatment of HIV-1 infection in a subject by administering triglyceride of conjugated linoleic acid and a thiol-containing compound. The Examiner has rejected Claim(s) 21 (in part), 22-24, 28-29, 32 (in part), 33-35, and 39-40 under 35 U.S.C. 103(a) as being allegedly unpatentable over McCleary (US Patent Application 2002/0132219A1, hereinafter "McCleary"). As cited by the Examiner, McCleary teaches:

1. [in Abstract] A nutritional supplement composition comprising conjugated linoleic acid and alpha-lipoic acid for ***modulating nutrient composition*** (emphasis added) in a human.

2. [¶0002] Disorders of nutrient partition include obesity (fat maldistribution) and hyperlipidemia.

3. [¶0006 to ¶0007] More particularly, it is desirable to provide a means for modulating aberrant pathways of nutrient partitioning so as to ***avoid excessive fat storage***, to ***promote oxidation of fat***, and ***reduce fat levels***.

4. [¶0010] McCleary also discloses specifically triglyceride of conjugated linoleic acid.

5. [¶0023] McCleary also teaches that ***fat synthesis*** and ***storage*** are diminished resulting in a fall in the intracellular fat content of the liver, pancreas, and skeletal muscle as well as a fall in visceral fat and ***total body fat stores*** accompanied by a decrease in individual fat cell volume.

6. [Table 1] Preferred amounts for CLA are 50 mg to 20 g and for alpha-lipoic acid are 25 mg to 2 g.

As noted by the Examiner, McCleary fails to disclose fat maldistribution or hyperlipidemia resulting from anti-retroviral treatment of HIV-1 infection in a subject. Specifically, in ¶0002 McCleary does not define obesity parenthetically as fat maldistribution and the term "fat maldistribution" never appears in the application. The term obesity is not defined in McCleary, but examples of generally accepted definitions of obesity by those skilled in the art are, "an excess proportion of total body fat" (http://www.webmd.com/diet/what-is-obesity) or, "a heavy accumulation of fat in the body's fat cells to such a serious degree that it rapidly increases the risk of obesity-associated diseases and mortality. The fat may be equally distributed on the body, on the stomach (apple-shaped) or on the hips and thighs (pear-shaped)" (http://www.netdoctor.co.uk/health_advice/facts/obesity.htm).

Maldistribution of fat with HIV/AR-related lipodystrophy as defined in [¶0008] of the instant application is, "typically a mix of ***central fat accumulation*** and ***peripheral fat loss***, and this pattern does not seem to fit readily into any definition of previously described lipodystrophies". Further in [¶0010], The physical changes associated with the HIV/ART lipodystrophy syndrome can be divided into two major types, both of which involve an abnormal or maldistribution of body fat: lipoatrophy or ***fat wasting*** and

lipohypertrophy or fat accumulation. An increase in abdominal girth is a common complaint in patients, while ***thinning of the extremities*** is also frequently seen, often with prominence of the veins in the arms and legs (cabling) due to ***subcutaneous fat loss***. A substantial proportion of patients report increased wrinkling of the skin with a ***loss of subcutaneous tissue in the cheeks and around the nose and lips***.

It is obvious from McCleary's teachings cited by the Examiner that the formulation described was specifically designed to ***promote oxidation of fat, reduce fat levels*** [¶0006 to ¶0007] including ***total body fat stores*** accompanied by a ***decrease in individual fat cell volume*** [¶0023]. A loss of total body fat stores as taught by McCleary, which would include peripheral fat, would severely exacerbate HIV/AR-related lipoatrophy. Thus, McCleary teaches away from and does not teach or suggest the prevention, treatment or normalization of fat maldistribution resulting from anti-retroviral treatment of HIV-1 infection in a subject (Claim 21 of the instant application).

Hyperlipidemia, as defined by McCleary, is limited to "postprandial hyperlipidemia" [¶0002] not to fasting hyperlipidemia. In the instant application, the term "hyperlipidemia" refers to a pathognomic condition manifest by elevated (fasting) serum concentrations of total cholesterol (>200 mg/dL), LDL cholesterol (>130 mg/dL), or triglycerides (>150 mg/dL) or decreased HDL cholesterol (<40 mg/dL) [¶0029]. A person having ordinary skill in the art recognizes the normal cutoff values presented are based on blood sampling conducted in the fasting state and used especially for disease evaluation. Postprandial hyperlipidemia is generally used to describe abnormal clearance of chylomicron triglycerides and combines a concentration variable (mg/dL) over an arbitrary time period (hr) frequently reported as area-under-the-curve (mg-hr/dL) after a

standard meal. Therefore, McCleary does not teach or suggest the treating, preventing or normalizing (fasting) hyperlipidemia resulting from anti-retroviral treatment of HIV-1 infection in a subject (Claim 32).

Further, McCleary fails to list any viral disease or drug toxicities as a "disorder of nutrient partitioning" in ¶0002. Included among the non-limiting list of "disorders of nutrient partitioning" in ¶0002 of McCleary are "insulin resistance, hyperinsulinemia, Syndrome X, hypertriglyceridemia and/or low HDL syndrome, high RQ (respiratory quotient) syndrome, obesity, chronic fatigue syndrome, small dense LDL syndrome, recidivism from weight loss, glucolipoxia, premature aging, memory loss, endothelial dysfunction, vascular disease, hypertension, postprandial hyperlipidemia, certain types of cancer, metabolic inflexibility and others." McCleary concludes in ¶0002, "The basic abnormality is similar in each circumstance but manifest clinically in different ways depending upon the organ involved, the individual's genetic makeup, age, sex and other factors." Since McCleary teaches that the basic abnormality of "disorders of nutrient partitioning" is the same for all of the listed manifestations, one of ordinary skill in the art would not infer that either HIV-1 infection or treatment with anti-retroviral drugs is the basic abnormality of McCleary's defined "disorders of nutrient partitioning". Nor would it be inferred by one of ordinary skill in the art that HIV-1 infection or treatment with anti-retroviral drugs is a manifestation of some pre-existing, basic abnormality.

Clearly the etiology of "disorders of nutrient partitioning" as defined by McClearly is unrelated to "disorders resulting from the interaction of an infectious agent and therapy against that infections agent" as defined in ¶0051 of the instant application. With uncommon etiologies, it is unlikely that one of ordinary skill in the art would be

sufficiently motivated to modify or combine the reference with a sufficient likelihood of successfully making the combination asserted.

Also noted by the Examiner, "Applicants' disclosure of the prior art teaches that HIV infection is accompanied by disturbances in lipid and glucose metabolism. These metabolic abnormalities are further confounded by hypercholesterolemia, hypertriglyceridemia, and hyperlipidemia induced by anti-retroviral drugs. In fact, it is estimated that almost two-thirds of HIV/AIDS patients exhibit abnormal fat distribution coincident with AR-therapy [¶0003 to 0009];" and the Examiner concludes, "Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to administer a nutritional supplement composition comprising conjugated linoleic acid and alpha-lipoic acid to treat a subject with fat maldistribution and hyperlipidemia resulting from anti-retroviral treatment of HIV-1 infection."

As previously discussed, what McCleary teaches is a composition containing conjugated linoleic acid and lipoic acid for reducing ***postprandial*** hyperlipidemia and ***total body fat*** regardless of location in the body. While, insulin resistance, hyperinsulinemia, Syndrome X and hypertriglyceridemia are listed as "disorders of nutrient partitioning" in ¶0002 of McCleary, they are also described as manifestations of a basic abnormality found in 30% to 50% of populations of westernized societies [¶0005]. As such, the etiology of McCleary's disorders of nutrient partitioning is unrelated to HIV-1 infection or therapy associated with HIV-1 infection; and it would, therefore, not be obvious for one of ordinary skill in the art to administer a nutritional supplement composition comprising conjugated linoleic acid and alpha-lipoic acid to

treat a subject with fat maldistribution and hyperlipidemia resulting from anti-retroviral treatment of HIV-1 infection.

Additionally, McCleary is a self-described weight loss program [¶0024] that functions to decrease total body fat and decrease appetite [¶0025]. The present invention does not function to reduce body weight or indiscriminately reduce body fat. Since wasting, or loss of body weight and appetite, is a constant concern in HIV patients, formulations that would cause a loss of body weight and appetite would be contraindicated and not considered rational treatment by persons of ordinary skill in the art. Further, the process of reversing fat maldistribution as seen in HIV/ART requires subcutaneous fat deposition in concert with visceral fat loss [¶0051]. McCleary describes a formulation containing conjugated linoleic acid and alpha-lipoic acid for the reduction of total body fat, while the claims in the instant application reflect a formulation that results in a targeted redistribution of body fat - a loss of visceral fat while maintaining or increasing subcutaneous fat. The fat maldistribution with HIV/AR-related lipodystrophy is typically a mix of central fat accumulation and peripheral fat loss, and this pattern does not seem to fit readily into any definition of previously described lipodystrophies [¶0008].

Thus, the facts that McCleary is a weight loss program that reduces total body fat and suppresses appetite teaches away from the usefulness of a formulation containing conjugated linoleic acid and lipoic acid for the treatment of fat maldistribution resulting from anti-retroviral treatment of HIV-1infection in a subject.

As further evidence of McCleary's lack of consideration of HIV-1 associated fat maldistribution, McCleary suggests participation in a blood donation program for optimal

effectiveness of the method [Abstract, ¶0060]. As described by McCleary, "Blood may be given about every 56 days." Since people living with HIV-1 infection are prohibited from donating blood, McCleary teaches away from considering use of his method for HIV-1 related disorders.

It is thus the Applicant's assertion that McCleary or a modification of McCleary does not teach or suggest each and every element of the present invention. Specifically, support for this conclusion comes from the following:

1. Fat maldistribution as specifically defined in the instant invention as an increase in visceral fat and a decrease in peripheral, subcutaneous fat is not mentioned or addressed in McCleary, which teaches a decrease in total body fat regardless of location in the body.
2. The method of McCleary suppresses appetite, a condition unwanted in persons with HIV-1 infection.
3. The hyperlipidemia defined in McCleary is postprandial not fasting hyperlipidemia and unrelated to hyperlipidemia as defined in the instant application.
4. McCleary states that the basic abnormality (etiology) is similar in each of the "disorders of nutrient partitioning" and can be found in 30% to 50% of the population of westernized society.
5. The method of using the formulation described by McCleary includes an optional blood donation program for optimal effectiveness. Thus, indicating McCleary had no intention of addressing HIV-1 associated fat maldistribution.

## CONCLUSION

In view of the foregoing, the Applicants assert that Claims 21-24, 28, 29, 32-35, 39 and 40 of the present application present allowable subject matter and the allowance thereof are requested. If any impediment to the allowance of these claims remains after consideration of the present amendment and above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone Dr. John G. Babish so that such issues may be resolved as expeditiously as possible.

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Respectfully submitted,

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